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ACID-CATALYZED IODINATION OF A HINDERED ALKYL ARYL KETONE: 2,4,6-TRIMETHYLACETOPHENONE (1). RATE DEPENDENCE ON IODINE CONCENTRATION

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Abstract- Rates of the perchloric and hydrochloric acid-catalyzed reactions of iodine with the title ketone (1) in 50% aqueous acetic acid at constant ionic strength were studied by following the decrease in iodine concentration at 353 nm. The rates were first order in iodine at concentrations up to about 6×10^{-5} M and first order in ketone concentration. A slight decrease in rate with increase in iodine concentration was attributed to complexation of iodine with the carbonyl oxygen. The effect of perchloric acid concentration on the rate was studied; a plot of k vs. [$HClO_4$] was bell-shaped with a maximum at about 9×10^{-3} M. Reversibility of the iodination reaction is suggested. Explanations are proposed for anomalous results observed in the effect of iodide concentration on the rate. E_a for the iodination reaction (82 kJ mol^{-1}) is higher than that for bromination of 1 in accord with the order for halogenation of other organic substrates.

In a previous investigation[1] the rate of the acid-catalyzed reaction of bromine with 2,4,6-trimethylacetophenone (1) was found to depend on bromine concentration at moderately high concentrations. This finding contrasts with usual observations in which rates of halogenation of ketones are dependent on concentrations of ketone and acid (or base) but are independent of halogen concentration and nature of halogen except predictably[2] at very low halogen concentrations. According to the generally accepted Lapworth mechanism[3] for normal reactions, the rate-determining step is conversion of ketone to enol (or enolate in base-catalyzed reactions) followed by rapid reaction with halogen. In the mechanism proposed for the anomalous reaction of bromine with 1, the enolization step was postulated to be fast, the rate-determining step being reaction of bromine with enol. It was of interest to investigate the acid-catalyzed reaction of iodine with 1[4]; the present paper reports the results of this study.

EXPERIMENTAL

The iodination was followed by measuring the decrease in absorbance of iodine with time by the same techniques[1] as with bromination. A wavelength of 353 nm was chosen; at this wavelength iodine solutions have maximum absorbances. Solutions of iodine followed Beer's law in the concentration range used for the kinetic study. At an ionic strength of 0.2 M (KCl), the molar absorptivity (ε) for the iodine-triiodide system (Table 1) was determined to be 28,200.

Since the ε value is very high, only relatively low concentrations of iodine (10^{-5}-10^{-4} M) could be used for the reaction. The reaction was conducted at a constant ionic strength of 0.20 M, adjusted either with KCl or $NaClO_4$. The reaction was initiated by introducing a solution of the pure ketone into the

Table 1. Ultraviolet Spectra of Iodine-triiodide System[a]

10^5 $[I_2]$ M	A	ε
0.7063	0.21	
1.413	0.41	
3.530	1.00	28,200
4.791	1.35	
6.063	1.70	

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[a] λ = 353 nm; [HCl] = 0.010 M; [KI] = 0.020 M; ionic strength (μ) = 0.20 M; temp. = 25.0° C; solvent = 50% AcOH (v/v).

potassium iodide in the reaction medium during the period of reaction. All reactions were carried out in the presence of 0.020 M potassium iodide. For each reaction, absorbance values were recorded up to about 80% of the reaction. Hydrochloric or perchloric acids were used for catalysis.

RESULTS AND DISCUSSION

The following observations were made based upon preliminary investigations:

1. There was an induction period for iodination even in the presence of H^+.
2. The induction period was eliminated with a large excess of ketone over iodine.
3. Not all iodine was consumed even with a high ketone:iodine ratio.
4. The rate of reaction slowed dramatically after about 70% of reaction.
5. At high concentrations of perchloric acid catalyst the reaction did not proceed beyond 10-20 %.
6. The reaction followed satisfactory first-order kinetics only at high concentrations of the ketone over that of iodine.

Effect of Iodine Concentration on Rate of Iodination. The data are in Table 2.

Table 2. Effect of Iodine Concentration on Rate of Iodination of 2,4,6-Trimethylacetophenone (1)[a]

$10^5[I_2]$ M	$10^3k_{obsd}/s^{-1}$
1.65	8.08
2.62	4.98
3.19	2.81
3.70	2.63
4.00	2.54
4.54	2.29
5.53	1.62
5.91	0.844

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[a] [Ket] = concentration of ketone (1) = 0.200 M; [HCl] = 0.010 M; [KI] = 0.020 M; temp. = 25.0° C; solvent = 50% AcOH (v/v); μ = 0.20 M

The iodination of 2,4,6-trimethylacetophenone (1) like its bromination, obeyed first-order kinetics with respect to iodine concentration (linear up to about 70% of reaction)(Fig 1). Beyond about 70% a slight deviation from a first-order

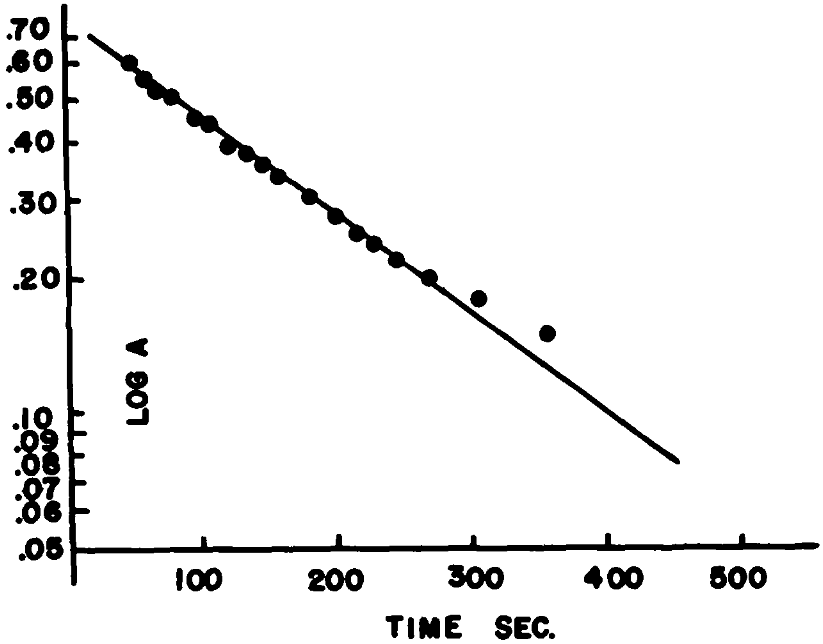
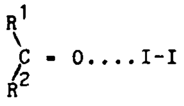


FIGURE I. FIRST-ORDER DEPENDENCE ON IODINE CONCENTRATION OF ACID-CATALYZED IODINATION OF ACETOMESITYLENE.

pattern was observed. The decrease in absorbance beyond this point was less than what would be expected. Iodination, unlike bromination or chlorination, is frequently reversible with several organic substrates as noted by many investigators. In the present study a small amount of iodine remained even after a long reaction time; it is evident that iodination of 2,4,6-trimethylacetophenone is reversible. Reversibility of iodination of menthone was observed by Bartlett and Vincent[10] who added an oxidizing agent to convert iodide to iodine, a technique later adopted by Zucker and Hammett[4]. Reversibility might account for the deviation in the kinetic pattern toward the end of the reaction studied in the present investigation.

Although each reaction studied conformed to first-order kinetics, the k_{obsd} values were not independent of the initial concentration of iodine. As the iodine concentration was increased, a decrease in rate constant was observed. The retarding influence by iodine may be due to the formation of a ketone-iodine complex (2). The formation of such a complex is well-substantiated[11] spectroscopi-



$$R^1R^2C=O\cdots I-I$$

2

cally. Such a complexation would make the ketone less active as compared with a "free" ketone molecule. Thus as $[I_2]$ increases, the concentration of active ketone molecules would decrease and this would result in a decreased rate constant.

Effect of Ketone Concentration on the Rate. The reaction was found to be first-order in ketone; the data are in Table 3. A plot of log k_{obsd} against log [K] gave a straight line with unit slope (Fig 2).

Table 3. Effect of Ketone Concentration on Rate of Reaction of Iodine with 2,4,6-Trimethylacetophenone (1)[a]

[Ket] M	$10^3\ k_{obsd}/s^{-1}$	$\frac{10^2\ k_{obsd}}{[K]}$ /l $mol^{-1}s^{-1}$
0.080	0.969	1.21
0.110	1.41	1.28
0.130	1.59	1.22
0.145	1.90	1.31
0.172	2.12	1.23
0.180	2.25	1.25
0.200	2.54	1.27

[a] $[I_2]$ = 4.00×10^{-5} M; [HCl] = 0.010 M; [KI] = 0.020 M; temp. = 25.0° C; solvent = 50% AcOH (v/v); μ = 0.20 M

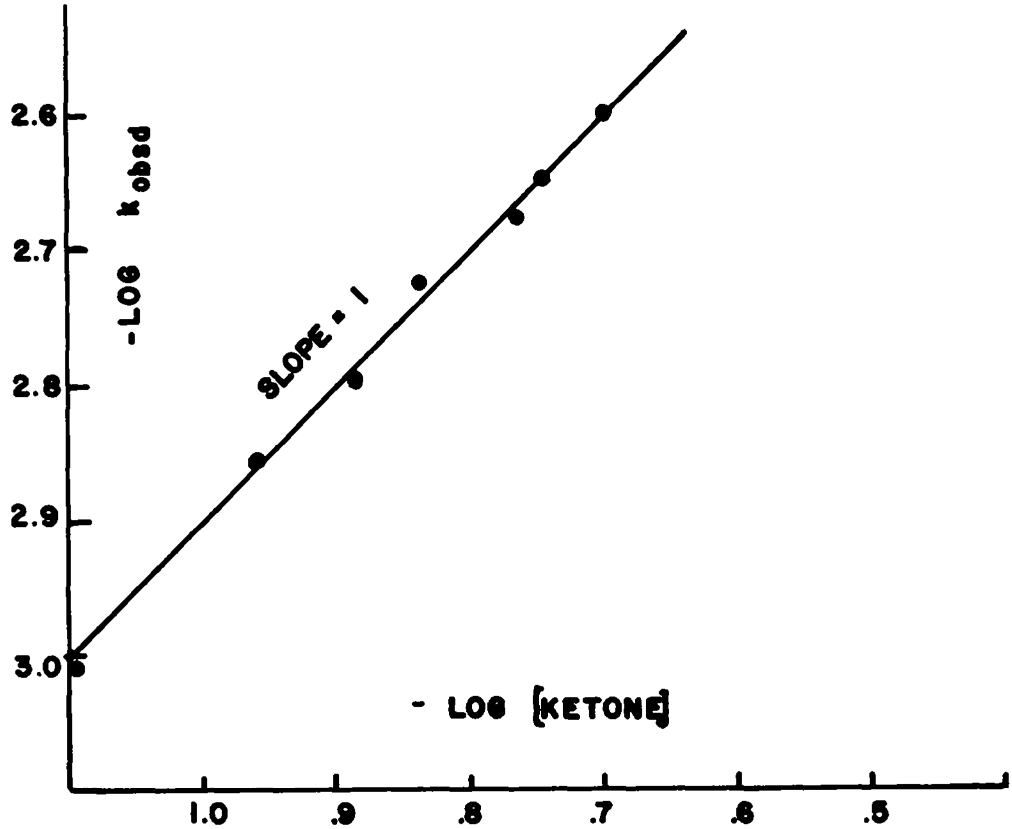


FIGURE 2. DEPENDENCE OF RATE ON KETONE CONCENTRATION OF ACID-CATALYZED IODINATION OF ACETOMESITYLENE.

Effect of Acid Concentration on Reaction Rate. The reaction was performed at various perchloric acid concentrations; the k_{obsd} values thus obtained are in Table 4. These values can be compared with the k value of 1.625×10^{-3} min^{-1} reported by Zucker and Hammett[4] for iodination of 1 in 1.388 M perchloric acid at 25.00°C.

Table 4. Effect of Perchloric Acid Concentration on Rate of Reaction of Iodine with 2,4,6-Trimethylacetophenone (1)[a]

$[HClO_4]$ M	$10^3\ k_{obsd}/s^{-1}$
0.000500	1.71
0.00200	1.82
0.00300	1.89
0.00600	2.38
0.00900	2.69
0.0120	2.62
0.0140	2.17
0.0160	1.78
0.0200	1.48
0.090	k values irregular

[a] [Ket] = 0.200 M; $[I_2]$ = 4.00 x 10^{-5} M; [KI] = 0.020 M; temp. = 25.0° C; solvent = 50% AcOH (v/v); μ = 0.20 M

These k_{obsd} values, when plotted against $[HClO_4]$ gave a bell-shaped profile (Fig 3). This indicates that the iodination is favored only in an intermediate range of perchloric acid concentrations selected for this study. The range favoring the reaction is relatively narrow. This trend may be explained by assuming that at low perchloric acid concentration the catalytic factor is small while at high perchloric acid concentration the reversible reaction becomes dominant. The latter assumption is strengthened by the observation that at $[HClO_4]$ = 0.090 M there was only about a 25% decrease in absorbance several hours after initiating the reaction.

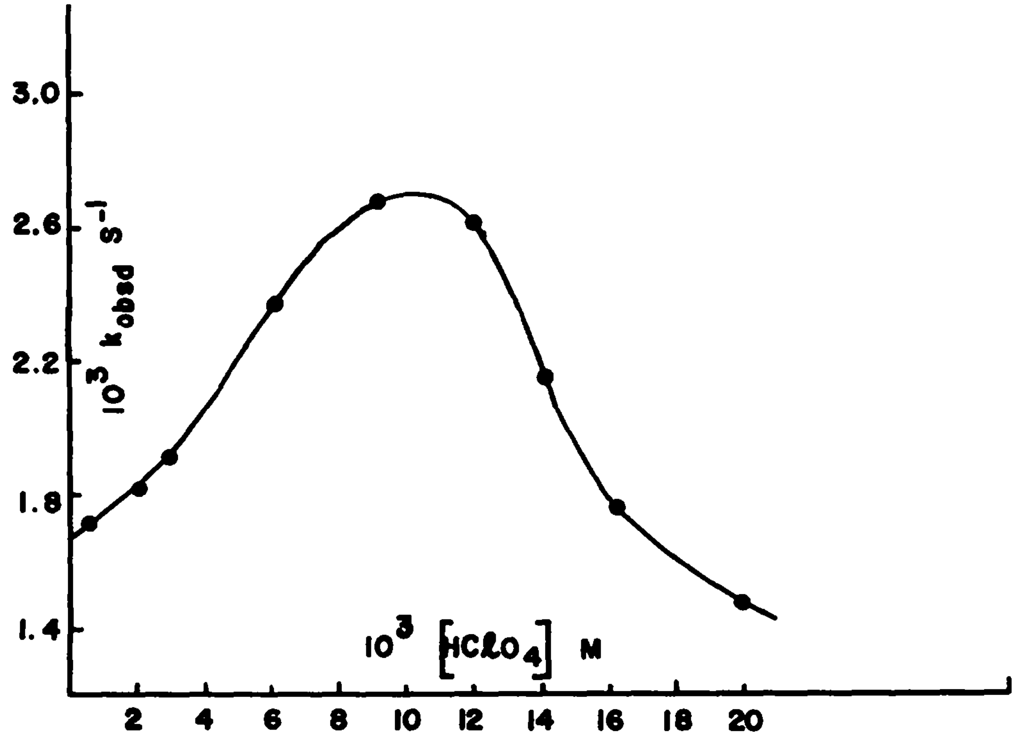


FIGURE 3. EFFECT OF PERCHLORIC ACID CONCENTRATION ON RATE OF ACID-CATALYZED IODINATION OF ACETOMESITYLENE.

Effect of Iodide Ion. In the previous study, bromide ion was found to influence the bromination of 2,4,6-trimethylacetophenone markedly. Hence it was anticipated that iodide ion might have a similar influence on iodination. To test this hypothesis the reaction was conducted with different initial concentrations of iodide. The ionic strength was adjusted to a constant value, 0.20 M, with sodium perchlorate. The k_{obsd} values are in Table 5.

Table 5. Effect of Iodide Ion on Rate of Acid-catalyzed Iodination of 2,4,6-Trimethylacetophenone (1)

[KI] M[a]	$10^3 k_{obsd}/s^{-1}$	
0.025	2.15	
0.020	2.67	satisfactory 1st order
0.017	2.78	
0.015	2.89	
0.012	3.01	1st order with considerable deviation
0.010	3.12	
[KI]	$10^8 k_0/mol\ l^{-1}\ s^{-1}$	
0.008	7.41	
0.006	8.00	satisfactory zero order
0.004	9.68	
0.002	10.1	excellent zero order

[a] [Ket] = 0.200 M; [$HClO_4$] = 0.010 M; [I_2] = 4.00×10^{-5} M; temp. = 25.0° C; μ = 0.20 M

When [KI] > 0.025 M, reaction did not proceed after about 25%; when [KI] < 0.002 M, iodine was incompletely dissolved. An anomalous trend in kinetics was observed on changing iodide ion concentration. As the concentration of iodide ion was decreased from 0.025 M to 0.002 M a transition in the order of the reaction was observed; the order changed from first to zero. Thus when [I^-] = 0.0020 M, the reaction followed excellent zero-order kinetics. With increasing iodide concentration, the reaction tended to follow first order kinetics. This unique trend in the kinetic pattern may be explained in terms of the iodine-iodide equilibrium and the relative reactivities of molecular iodine and the triiodide ion.

$$I_2 + I^- = I_3^-$$

The order of halogenation (iodination) depends upon the relative rates of enolization and halogenation. Generally, with most ketones the reaction follows a zero order in halogen. It might be expected that when the halogenation step becomes slower than enolization, the kinetics would follow a first order in halogen. The rate of halogenation would in turn depend upon the nature of the halogen species in the reaction medium. In the present investigation, possible iodine species are molecular iodine and triiodide ion. The concentration of I_3^- is expected to increase with increasing concentration of iodide ion. Hence, at high [I^-] almost all of the molecular iodine would be expected to exist as I_3^- and under this condition I_3^- would be the iodinating species. When [I^-] is low, the concentration of I_3^- is likely to be low and hence, molecular iodine would be the predominant iodinating species. Under these circumstances, if one assumes that I_3^- is a less active halogenating entity compared to I_2, the rate of iodination with I_3^- should be less than that with I_2. The rate of iodination with I_3^- may be so slow as to make it slower than the rate of enolization. This would lead to a first-order dependence in iodine. At low $[I^-]$ the iodination involving molecular iodine should be faster than enolization and consequently, the order becomes zero with respect to iodine concentration. The entire argument is based on the assumption that triiodide ion is a less effective halogenating species than molecular iodine. This is strongly supported by the trend in the rate constants with the change in $[I^-]$; as $[I^-]$ is decreased, both first- and zero-order constants are enhanced.

Effect of Temperature. To evaluate activation parameters and compare them with those previously obtained for bromination, the reaction was conducted at six temperatures in the range, 9.3-29.0° C. The rate values thus obtained are in Table 6.

Table 6. Effect of Temperature on Rate of Acid-catalyzed Iodination of 2,4,6-Trimethylacetophenone (1)[a]

Temp (°C)	$10^3\ k_{obsd}/s^{-1}$	$k_2/l\ mol^{-1}\ s^{-1}$
9.3	0.383	0.00192
17.8	1.15	0.00575
22.0	1.81	0.00905
23.8	2.23	0.01120
25.0	2.54	0.01270
29.0	3.63	0.01805

$[Ket] = 0.200\ M$; $[HCl] = 0.010\ M$; $[I_2] = 4.00 \times 10^{-5}\ M$; $[KI] = 0.020\ M$; solvent = 50% AcOH (v/v); $\mu = 0.20\ M$.

A plot of ln k_2 versus 1/T was linear (correlation coefficient = 0.9919).

$$E_a = 82 \pm 3\ kJ\ mol^{-1}$$
$$\Delta H^{\ddagger} = 79.5 \pm 3\ kJ\ mol^{-1}$$

These values may be compared with those for bromination of 2,4,6-trimethylacetophenone. E_a for bromination (61.5 ±3 kJ mol^{-1}) was lower than that for iodination. This indicates that iodination is less facile than bromination. This observation agrees with the general and well-established relative reactivities of bromine and iodine with organic substrates, namely that iodination is sluggish and reversible while bromination is more facile and relatively less reversible.

For strict comparison, the two halogenations should be carried out under identical conditions. However, several attempts to do so were unsuccessful. Because of the high absorptivity[6] of triiodide ion, the iodine concentration for the reaction had to be of the order of 10^{-5} M. When $[I_2]$ was greater than 10^{-5} M the absorbance was off the spectrometer scale. Tribromide ion, on the other hand has a relatively low absorptivity which necessitated the use of relatively high concentrations of bromine of the order of 10^{-3} M. When the bromine concentration was less than 10^{-3} M the absorbance fell below 0.2 A and the reaction could not be followed spectrophotometrically.

In summary, the rate of the acid-catalyzed iodination of 2,4,6-trimethylacetophenone is first-order in iodine at moderate iodine concentrations analogous to previous results with bromination. The energy of activation for iodination is higher than that for bromination. In addition, iodination does not go to completion because of the reverse reaction with hydrogen iodide as compared with the bromination of 1.

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4. The rate of reaction of iodine with 1 was previously studied by Zucker and Hammett [5]; however, their studies were in much more concentrated perchloric acid, 1.388 M and mainly concerned with acetophenone and derivatives. In addition, they did not report any dependence on iodine concentration.
5. L. Zucker and L. P. Hammett, **J. Am. Chem. Soc.**, 1939, 61, 2779-2784.
6. The use of wavelengths other than ε_{max} at 353 nm was considered at a later stage of this investigation in order to be able to increase the iodine concentration. It would be worthwhile to carry out this modification in order to obtain a better comparison with the earlier[1] bromination results. This suggestion was also made by one of the referees.
7. Both referees pointed out that $\ln(A-A_\infty)$ vs. t can be plotted in cases where the reaction is reversible. With the relatively low acid concentrations used in this study (0.01 to 0.02 M) good linear ln A vs. t plots were obtained up to about 70% of the reactions with reactions being followed out to about 80% for all reactions studied. Figs 1 and 2 are examples of the types of plots obtained. Earlier deviation from linearity was only observed in the case where the perchloric acid concentration was much higher (0.09 M, Table 4) where the $\ln(A-A_\infty)$ plot would be needed. It was suggested that if the $\ln(A-A_\infty)$ plot were used for the Table 4 data, $k_1 + k_{-1}$ could be obtained[8]. Then knowing A_∞, k_1 and k_{-1} could be obtained separately and the k_1 thus obtained should increase linearly with [$HClO_4$] instead of the bell-shaped curve in Fig 3. Another suggestion was that if one were to start with the iodinated product at the higher acid concentration, the formation of iodine could be noted, thus checking the formation of an equilibrium mixture. The expected monoiodinated product, 2-iodo-2',4',6'-trimethylacetophenone, is available since it was previously[9] prepared by reacting acetomesitylene with an iodine/KI mixture. These would be worthwhile further experiments to carry out. It should be noted that in the case of the bromination studies[1] the corresponding monobrominated product was isolated from a larger-scale preparation under reaction conditions and characterized.
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